

# PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
US Department of Commerce  
United States Patent and Trademark  
Office, PCT  
2011 South Clark Place Room  
CP2/5C24  
Arlington, VA 22202  
ETATS-UNIS D'AMERIQUE  
in its capacity as elected Office

Date of mailing:

25 January 2001 (25.01.01)

International application No.:

PCT/JP00/04830

Applicant's or agent's file reference:

2624WO0P

International filing date:

19 July 2000 (19.07.00)

Priority date:

21 July 1999 (21.07.99)

Applicant:

OJIMA, Mami et al

1. The designated Office is hereby notified of its election made:



in the demand filed with the International preliminary Examining Authority on:

23 August 2000 (23.08.00)



in a notice effecting later election filed with the International Bureau on:

2. The election



was



was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

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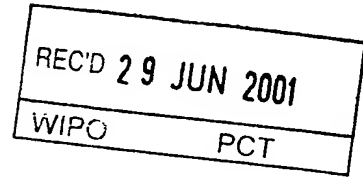
14T

特 許 協 力 条 約

PCT

国際予備審査報告

(法第12条、法施行規則第56条)  
[PCT36条及びPCT規則70]



出願人又は代理人 の書類記号 2624W00P	今後の手続きについては、国際予備審査報告の送付通知(様式PCT/ IPEA/416)を参照すること。	
国際出願番号 PCT/JPO0/04830	国際出願日 (日.月.年) 19.07.00	優先日 (日.月.年) 21.07.99
国際特許分類(IPC) Int. Cl <sup>7</sup> A61K45/00, 31/4188, 31/4245, A61P25/28, 9/10		
出願人(氏名又は名称) 武田薬品工業株式会社		

1. 国際予備審査機関が作成したこの国際予備審査報告を法施行規則第57条(PCT36条)の規定に従い送付する。
2. この国際予備審査報告は、この表紙を含めて全部で 5 ページからなる。
- ☐ この国際予備審査報告には、附属書類、つまり補正されて、この報告の基礎とされた及び/又はこの国際予備審査機関に対してした訂正を含む明細書、請求の範囲及び/又は図面も添付されている。  
(PCT規則70.16及びPCT実施細則第607号参照)  
この附属書類は、全部で          ページである。

3. この国際予備審査報告は、次の内容を含む。

- I ☒ 国際予備審査報告の基礎
- II ☐ 優先権
- III ☒ 新規性、進歩性又は産業上の利用可能性についての国際予備審査報告の不作成
- IV ☐ 発明の単一性の欠如
- V ☒ PCT35条(2)に規定する新規性、進歩性又は産業上の利用可能性についての見解、それを裏付けるための文献及び説明
- VI ☐ ある種の引用文献
- VII ☐ 国際出願の不備
- VIII ☐ 国際出願に対する意見

国際予備審査の請求書を受理した日 23.08.00	国際予備審査報告を作成した日 11.06.01	
名称及びあて先 日本国特許庁(IPEA/JP) 郵便番号100-8915 東京都千代田区霞が関三丁目4番3号	特許庁審査官(権限のある職員) 森井 隆信	4C 2938
	電話番号 03-3581-1101 内線 6460	

様式PCT/IPEA/409(表紙)(1998年7月)

## I. 国際予備審査報告の基礎

1. この国際予備審査報告は下記の出願書類に基づいて作成された。(法第6条(PCT14条)の規定に基づく命令に  
応答するために提出された差し替え用紙は、この報告書において「出願時」とし、本報告書には添付しない。  
PCT規則70.16, 70.17)

☒ 出願時の国際出願書類

- |                                     |                |                      |
|-------------------------------------|----------------|----------------------|
| <input type="checkbox"/> 明細書        | 第 _____ ページ、   | 出願時に提出されたもの          |
| <input type="checkbox"/> 明細書        | 第 _____ ページ、   | 国際予備審査の請求書と共に提出されたもの |
| <input type="checkbox"/> 明細書        | 第 _____ ページ、   | 付の書簡と共に提出されたもの       |
| <input type="checkbox"/> 請求の範囲      | 第 _____ 項、     | 出願時に提出されたもの          |
| <input type="checkbox"/> 請求の範囲      | 第 _____ 項、     | PCT19条の規定に基づき補正されたもの |
| <input type="checkbox"/> 請求の範囲      | 第 _____ 項、     | 国際予備審査の請求書と共に提出されたもの |
| <input type="checkbox"/> 請求の範囲      | 第 _____ 項、     | 付の書簡と共に提出されたもの       |
| <input type="checkbox"/> 図面         | 第 _____ ページ/図、 | 出願時に提出されたもの          |
| <input type="checkbox"/> 図面         | 第 _____ ページ/図、 | 国際予備審査の請求書と共に提出されたもの |
| <input type="checkbox"/> 図面         | 第 _____ ページ/図、 | 付の書簡と共に提出されたもの       |
| <input type="checkbox"/> 明細書の配列表の部分 | 第 _____ ページ、   | 出願時に提出されたもの          |
| <input type="checkbox"/> 明細書の配列表の部分 | 第 _____ ページ、   | 国際予備審査の請求書と共に提出されたもの |
| <input type="checkbox"/> 明細書の配列表の部分 | 第 _____ ページ、   | 付の書簡と共に提出されたもの       |

2. 上記の出願書類の言語は、下記に示す場合を除くほか、この国際出願の言語である。

上記の書類は、下記の言語である \_\_\_\_\_ 語である。

- ☐ 国際調査のために提出されたPCT規則23.1(b)にいう翻訳文の言語  
☐ PCT規則48.3(b)にいう国際公開の言語  
☐ 国際予備審査のために提出されたPCT規則55.2または55.3にいう翻訳文の言語

3. この国際出願は、ヌクレオチド又はアミノ酸配列を含んでおり、次の配列表に基づき国際予備審査報告を行った。

- ☐ この国際出願に含まれる書面による配列表  
☐ この国際出願と共に提出されたフレキシブルディスクによる配列表  
☐ 出願後に、この国際予備審査(または調査)機関に提出された書面による配列表  
☐ 出願後に、この国際予備審査(または調査)機関に提出されたフレキシブルディスクによる配列表  
☐ 出願後に提出した書面による配列表が出願時における国際出願の開示の範囲を超える事項を含まない旨の陳述書の提出があった  
☐ 書面による配列表に記載した配列とフレキシブルディスクによる配列表に記載した配列が同一である旨の陳述書の提出があった。

4. 補正により、下記の書類が削除された。

- ☐ 明細書 第 \_\_\_\_\_ ページ  
☐ 請求の範囲 第 \_\_\_\_\_ 項  
☐ 図面 図面の第 \_\_\_\_\_ ページ/図

5. ☐ この国際予備審査報告は、補充欄に示したように、補正が出願時における開示の範囲を越えてされたものと認められるので、その補正がされなかったものとして作成した。(PCT規則70.2(c) この補正を含む差し替え用紙は上記1.における判断の際に考慮しなければならない、本報告に添付する。)

## III. 新規性、進歩性又は産業上の利用可能性についての国際予備審査報告の不作成

1. 次に関して、当該請求の範囲に記載されている発明の新規性、進歩性又は産業上の利用可能性につき、次の理由により審査しない。

☐ 国際出願全体

☒ 請求の範囲 14-15

理由:

☒ この国際出願又は請求の範囲 14-15 は、国際予備審査をすることを要しない次の事項を内容としている（具体的に記載すること）。

請求の範囲 14-15 は「治療による人体の処置方法に関するもの」であって、PCT 34 条(4) (a) (i) 及び PCT 規則 67.1 (iv) の規定により、この国際予備審査機関が国際予備審査をすることを要しない対象に係るものである。

☐ 明細書、請求の範囲若しくは図面（次に示す部分）又は請求の範囲 14-15 の記載が、不明確であるため、見解を示すことができない（具体的に記載すること）。

☐ 全部の請求の範囲又は請求の範囲 14-15 が、明細書による十分な裏付けを欠くため、見解を示すことができない。

☒ 請求の範囲 14-15 について、国際調査報告が作成されていない。

2. ヌクレオチド又はアミノ酸の配列表が実施細則の附属書 C（塩基配列又はアミノ酸配列を含む明細書等の作成のためのガイドライン）に定める基準を満たしていないので、有効な国際予備審査をすることができない。

☐ 書面による配列表が提出されていない又は所定の基準を満たしていない。

☐ フレキシブルディスクによる配列表が提出されていない又は所定の基準を満たしていない。

## V. 新規性、進歩性又は産業上の利用可能性についての法第12条(PCT35条(2))に定める見解、それを裏付ける文献及び説明

## 1. 見解

新規性(N)

請求の範囲 1-13, 16-17 有  
請求の範囲 無

進歩性(IS)

請求の範囲 有  
請求の範囲 1-13, 16-17 無

産業上の利用可能性(IA)

請求の範囲 有  
請求の範囲 1-13, 16-17 無

## 2. 文献及び説明(PCT規則70.7)

文献1: EP, 425921, A1(TAKEDA CHEMICAL INDUSTRIES, LTD.) 8.5月.1991  
(08.05.91)文献2: EP, 459136, A1(TAKEDA CHEMICAL INDUSTRIES, LTD.) 4.12月.1991  
(04.12.91) & US, 5328919, A文献3: 藤島正敏「脳血管障害の発症・再発とその予防」医歯薬出版株式会社、医学  
の歩み、Vol.188、No.4、23.1月.1999(23.01.99), pp217-222文献4: TAKAHASHI, Masaya et al, 'Therapeutic effects of imidapril on  
cerebral lesions observed by magnetic resonance imaging in malignant  
stroke-prone spontaneously hypertensive rats', Journal of Hypertension  
1994, Vol.12、No.7、pp761-768文献5: 長谷川恒雄「脳梗塞患者のリハビリテーションー機能評価とリハビリテーシ  
ョンの進め方ー」株式会社日本臨床社、CT, MRI時代の脳卒中学ー新しい診断・  
治療体系ー(上巻), 1993, pp505-508

補充欄 (いずれかの欄の大きさが足りない場合に使用すること)

## 第 V 欄の続き

請求の範囲 1-13、16-17 について

文献 1 及び 2 には、本願の請求の範囲 5-9 に記載のアンジオテンシン I I 拮抗作用を奏する化合物が記載されており、当該化合物は脳卒中の治療に用いられることが記載されている。

文献 3 には、脳卒中再発の危険因子は発症の危険因子と基本的に変わらないことが記載されている。

文献 4 には、ACE 阻害剤の 1 種である imidapril が脳卒中の再発予防作用を奏することが記載されている。

そして、文献 5 には、脳血管障害の後遺症として神経症状、運動障害、精神機能障害、日常生活動作障害等が記載されている。

文献 3 に記載のとおり、脳卒中の危険因子は発症の危険因子と基本的に変わらないと認められ、また文献 4 に記載のように、文献 1-2 に記載の化合物と同様にレニン-アンジオテンシン系を抑制し、アンジオテンシン I I の作用を抑制する降圧剤である ACE 阻害剤が脳卒中の治療だけでなく再発の予防作用も奏すると認められるところ、文献 1-2 に記載のとおり脳血管障害の治療に用いられる化合物を、脳血管障害の治療のみでなく再発予防に用いることは当該技術分野の専門家にとって自明である。

また、文献 5 に記載のような後遺症に対して用いることも当該技術分野の専門家にとって自明である。

そして、本願明細書において、請求の範囲 1-13、16-17 に記載の医薬が脳血管障害の再発防止剤または後遺症の改善・進展抑制剤として有用であることを裏付ける具体的な記載もない。

したがって、本願の請求の範囲 1-13、16-17 に係る発明は進歩性を有さない。

E P

US

P C T

## 国際調査報告

(法 8 条、法施行規則第40、41条)  
[P C T 1 8 条、P C T 規則43、44]

出願人又は代理人 の書類記号 2 6 2 4 W O O P	今後の手続きについては、国際調査報告の送付通知様式(P C T / I S A / 2 2 0 ) 及び下記 5 を参照すること。		
国際出願番号 P C T / J P 0 0 / 0 4 8 3 0	国際出願日 (日.月.年) 1 9 . 0 7 . 0 0	優先日 (日.月.年) 2 1 . 0 7 . 9 9	
出願人 (氏名又は名称) 武田薬品工業株式会社			

国際調査機関が作成したこの国際調査報告を法施行規則第41条 (P C T 1 8 条) の規定に従い出願人に送付する。  
この写しは国際事務局にも送付される。

この国際調査報告は、全部で 4 ページである。

☐ この調査報告に引用された先行技術文献の写しも添付されている。

## 1. 国際調査報告の基礎

a. 言語は、下記に示す場合を除くほか、この国際出願がされたものに基づき国際調査を行った。

☐ この国際調査機関に提出された国際出願の翻訳文に基づき国際調査を行った。

b. この国際出願は、ヌクレオチド又はアミノ酸配列を含んでおり、次の配列表に基づき国際調査を行った。

☐ この国際出願に含まれる書面による配列表

☐ この国際出願と共に提出されたフレキシブルディスクによる配列表

☐ 出願後に、この国際調査機関に提出された書面による配列表

☐ 出願後に、この国際調査機関に提出されたフレキシブルディスクによる配列表

☐ 出願後に提出した書面による配列表が出願時における国際出願の開示の範囲を超える事項を含まない旨の陳述書の提出があった。

☐ 書面による配列表に記載した配列とフレキシブルディスクによる配列表に記載した配列が同一である旨の陳述書の提出があった。

2. ☒ 請求の範囲の一部の調査ができない (第 I 欄参照)。

3. ☐ 発明の単一性が欠如している (第 II 欄参照)。

4. 発明の名称は ☒ 出願人が提出したものを承認する。

☐ 次に示すように国際調査機関が作成した。

5. 要約は ☒ 出願人が提出したものを承認する。

☐ 第 III 欄に示されているように、法施行規則第47条 (P C T 規則38.2(b)) の規定により国際調査機関が作成した。出願人は、この国際調査報告の発送の日から 1 カ月以内にこの国際調査機関に意見を提出することができる。

6. 要約書とともに公表される図は、  
第 \_\_\_\_\_ 図とする。 ☐ 出願人が示したとおりである。

☒ なし

☐ 出願人は図を示さなかった。

☐ 本図は発明の特徴を一層よく表している。

## 第Ⅰ欄 請求の範囲の一部の調査ができないときの意見（第1ページの2の続き）

法第8条第3項（PCT17条(2)(a)）の規定により、この国際調査報告は次の理由により請求の範囲の一部について作成しなかった。

1. ☒ 請求の範囲 14-15 は、この国際調査機関が調査をすることを要しない対象に係るものである。つまり、  
請求の範囲14-15は、治療による人体の処置方法に関するものであって、PCT第17条(2)(a)(i)及びPCT規則39.1(iV)の規定により、この国際調査機関が国際調査を行うことを要しない対象に係るものである。
2. ☐ 請求の範囲 は、有意義な国際調査をすることができる程度まで所定の要件を満たしていない国際出願の部分に係るものである。つまり、
3. ☐ 請求の範囲 は、従属請求の範囲であってPCT規則6.4(a)の第2文及び第3文の規定に従って記載されていない。

## 第Ⅱ欄 発明の単一性が欠如しているときの意見（第1ページの3の続き）

次に述べるようにこの国際出願に二以上の発明があるとこの国際調査機関は認めた。

1. ☐ 出願人が必要な追加調査手数料をすべて期間内に納付したので、この国際調査報告は、すべての調査可能な請求の範囲について作成した。
2. ☐ 追加調査手数料を要求するまでもなく、すべての調査可能な請求の範囲について調査することができたので、追加調査手数料の納付を求めなかった。
3. ☐ 出願人が必要な追加調査手数料を一部のみしか期間内に納付しなかったので、この国際調査報告は、手数料の納付のあった次の請求の範囲のみについて作成した。
4. ☐ 出願人が必要な追加調査手数料を期間内に納付しなかったので、この国際調査報告は、請求の範囲の最初に記載されている発明に係る次の請求の範囲について作成した。

追加調査手数料の異議の申立てに関する注意

- ☐ 追加調査手数料の納付と共に出願人から異議申立てがあった。  
☐ 追加調査手数料の納付と共に出願人から異議申立てがなかった。



## A. 発明の属する分野の分類 (国際特許分類 (IPC))

Int. Cl. A61K45/00, 31/4188, 31/4245, A61P25/28, 9/10

## B. 調査を行った分野

調査を行った最小限資料 (国際特許分類 (IPC))

Int. Cl. A61K45/00, 31/4188, 31/4245, A61P25/28, 9/10

最小限資料以外の資料で調査を行った分野に含まれるもの

日本国実用新案公報	1926-1996年
日本国公開実用新案公報	1971-2000年
日本国登録実用新案公報	1994-2000年
日本国実用新案登録公報	1996-2000年

国際調査で使用した電子データベース (データベースの名称、調査に使用した用語)

CAPLUS (STN)	EMBASE (STN)
MEDLINE (STN)	
BIOSIS (STN)	

## C. 関連すると認められる文献

引用文献の カテゴリー*	引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示	関連する 請求の範囲の番号
Y	EP, 425921, A1 (TAKEDA CHEMICAL INDUSTRIES, LTD.) 8.5月.1991 (08.05.91) 全文 & JP, 4-9373, A	1-13, 16-17
Y	EP, 459136, A1 (TAKEDA CHEMICAL INDUSTRIES, LTD.) 4.12月.1991 (04.12.91) 全文 & US, 5328919, A & JP, 8-99960, A	1-13, 16-17
Y	藤島正敏「脳血管障害の発症・再発とその予防」医歯薬出版株式会社、医学の歩み、第188巻、第4号、23.1月.1999 (23.01.99) pp217-222、全文	1-13, 16-17

☒ C欄の続きにも文献が列举されている。☐ パテントファミリーに関する別紙を参照。

## \* 引用文献のカテゴリー

「A」 特に関連のある文献ではなく、一般的技術水準を示すもの  
「E」 国際出願日前の出願または特許であるが、国際出願日以後に公表されたもの  
「L」 優先権主張に疑義を提起する文献又は他の文献の発行日若しくは他の特別な理由を確立するために引用する文献 (理由を付す)  
「O」 口頭による開示、使用、展示等に言及する文献  
「P」 国際出願日前で、かつ優先権の主張の基礎となる出願

の日の後に公表された文献

「T」 国際出願日又は優先日後に公表された文献であって出願と矛盾するものではなく、発明の原理又は理論の理解のために引用するもの

「X」 特に関連のある文献であって、当該文献のみで発明の新規性又は進歩性がないと考えられるもの

「Y」 特に関連のある文献であって、当該文献と他の1以上の文献との、当業者にとって自明である組合せによって進歩性がないと考えられるもの

「&amp;」 同一パテントファミリー文献

国際調査を完了した日

01.11.00

国際調査報告の発送日

14.11.00

国際調査機関の名称及びあて先

日本国特許庁 (ISA / JP)

郵便番号 100-8915

東京都千代田区霞が関三丁目4番3号

特許庁審査官 (権限のある職員)

森井 隆信

4C

2938

電話番号 03-3581-1101 内線 6460

C (続き) . 関連すると認められる文献		
引用文献の カテゴリー*	引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示	関連する 請求の範囲の番号
Y	TAKAHASHI, Masaya et al, 'Therapeutic effects of imidapril on cerebral lesions observed by magnetic resonance imaging in malignant stroke-prone spontaneously hypertensive rats' Journal of Hypertension (1994) 第12巻、第7号、pp761-768、全文	1-13, 16-17
Y	長谷川恒雄「脳梗塞患者のリハビリテーションー機能評価とリハビリテーションの進め方ー」株式会社日本臨床社、CT, MR I時代の脳卒中学ー新しい診断・治療体系ー(上巻)、24.11月.1993 (24.11.93)、pp505-508、全文	10-13

10/031,398 #5



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FAX +31 70 340 3016

**Europäisches  
Patentamt**

Zweigstelle  
in Den Haag  
Recherchen-  
abteilung

**European  
Patent Office**

Branch at  
The Hague  
Search  
division

**Office européen  
des brevets**

Département à  
La Haye  
Division de la  
recherche

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Patentanwälte  
Prinzregentenstrasse 116  
80538 München  
ALLEMAGNE

**LEDERER & KELLER**  
EINGANG / RECEIPT  
07.01.2003  
Erl.: .....

Datum/Date  
07.01.03

Zeichen/Ref./Réf. <b>662970</b>	Anmeldung Nr./Application No./Demande n°/Patent Nr./Patent No./Brevet n°. <b>00946393.6-2112-JP0004830</b>
Anmelder/Applicant/Demandeur/Patentinhaber/Proprietor/Titulaire <b>Takeda Chemical Industries, Ltd.</b>	

## COMMUNICATION

The European Patent Office herewith transmits as an enclosure the European search report for the above-mentioned European patent application.

If applicable, copies of the documents cited in the European search report are attached.

☒ Additional set(s) of copies of the documents cited in the European search report is (are) enclosed as well.

## REFUND OF THE SEARCH FEE

If applicable under Article 10 Rules relating to fees, a separate communication from the Receiving Section on the refund of the search fee will be sent later.



# INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP00/04830

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 14-15  
because they relate to subject matter not required to be searched by this Authority, namely:  
Claims 14 and 15 pertain to methods for treatment of the human body by therapy and thus relate to a subject matter which this International Searching Authority is not required, under the provisions of Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT, to search.
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐  
☐

- The additional search fees were accompanied by the applicant's protest.  
No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP00/04830

## A. CLASSIFICATION OF SUBJECT MATTER

Int.Cl<sup>7</sup> A61K45/00, 31/4188, 31/4245, A61P25/28, 9/10

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Int.Cl<sup>7</sup> A61K45/00, 31/4188, 31/4245, A61P25/28, 9/10

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Jitsuyo Shinan Koho 1926-1996 Toroku Jitsuyo Shinan Koho 1994-2000  
Kokai Jitsuyo Shinan Koho 1971-2000 Jitsuyo Shinan Toroku Koho 1996-2000

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAPLUS (STN) EMBASE (STN)  
MEDLINE (STN)  
BIOSIS (STN)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP, 425921, A1 (TAKEDA CHEMICAL INDUSTRIES, LTD.), 08 May, 1991 (08.05.91), Full text & JP, 4-9373, A	1-13, 16-17
Y	EP, 459136, A1 (TAKEDA CHEMICAL INDUSTRIES, LTD.), 04 December, 1991 (04.12.91), Full text & US, 5328919, A & JP, 8-99960, A	1-13, 16-17
Y	Masatoshi FUJISHIMA, "Nou Kekkan Shougai no Hasshou, Saihatsu to sono Yobou", Ishiyaku Shuppan K.K., Igaku no Ayumi, Vol.188, No.4, 23 January, 1999 (23.01.99) pp.217-222, Full text	1-13, 16-17
Y	TAKAHASHI, Masaya et al, 'Therapeutic effects of imidapril on cerebral lesions observed by magnetic resonance imaging in malignant stroke-prone spontaneously hypertensive rats' Journal of Hypertension (1994), Vol.12, No.7, pp.761-768, Full text	1-13, 16-17

☒ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

\* Special categories of cited documents:  
"A" document defining the general state of the art which is not  
considered to be of particular relevance  
"E" earlier document but published on or after the international filing  
date  
"L" document which may throw doubts on priority claim(s) or which is  
cited to establish the publication date of another citation or other  
special reason (as specified)  
"O" document referring to an oral disclosure, use, exhibition or other  
means  
"P" document published prior to the international filing date but later  
than the priority date claimed

"T" later document published after the international filing date or  
priority date and not in conflict with the application but cited to  
understand the principle or theory underlying the invention  
"X" document of particular relevance; the claimed invention cannot be  
considered novel or cannot be considered to involve an inventive  
step when the document is taken alone  
"Y" document of particular relevance; the claimed invention cannot be  
considered to involve an inventive step when the document is  
combined with one or more other such documents, such  
combination being obvious to a person skilled in the art  
"&" document member of the same patent family

Date of the actual completion of the international search  
01 November, 2000 (01.11.00)

Date of mailing of the international search report  
14 November, 2000 (14.11.00)

Name and mailing address of the ISA/  
Japanese Patent Office

Authorized officer

Facsimile No.

Telephone No.



European Patent  
Office

**SUPPLEMENTARY  
EUROPEAN SEARCH REPORT**

Application Number  
EP 00 94 6393

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X	SAAVEDRA J.M.: "THE ROLE OF ANGIOTENSIN II IN THE REGULATION OF CEREBROVASCULAR FUCNTION IN THE RAT" PHARM. PHARMACOL. LETT., vol. 3, 1994, pages 256-259, XP009000718 * abstract *	1-15	A61K45/00 A61K31/4188 A61K31/4245 A61P25/28 A61P9/10
X	SCHRADER J ET AL: "HYPERTENSION AND STROKE - RATIONALE BEHIND THE ACCESS TRIAL" BASIC RESEARCH IN CARDIOLOGY, STEINKOPFF, DARMSTADT, DE, vol. 93, no. SUPPL 2, 1998, pages 69-78, XP001019616 ISSN: 0300-8428	1-4,6, 10-15	
Y	* abstract * * page 74, right-hand column * * page 70, right-hand column - page 71, left-hand column *	5,7-9	
Y	DE 41 42 366 A (THOMAE GMBH DR K) 24 June 1993 (1993-06-24) * page 16, line 51 *	5,7-9	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
Y	EP 0 556 789 A (THOMAE GMBH DR K) 25 August 1993 (1993-08-25) * page 2; figure I *	5,7-9	A61K
X,P	WO 00 16773 A (HERBERT JEAN MARC ;SANOFI SYNTHELABO (FR); NISATO DINO (FR); CAZAU) 30 March 2000 (2000-03-30) * page 9; example 2 *	1-4,6, 10-15	
X,P	WO 00 02543 A (NOVARTIS ERFIND VERWALT GMBH ;NOVARTIS AG (CH); GASPARO MARC DE (C) 20 January 2000 (2000-01-20) * page 4, line 21 * * page 4, line 2 *	1-4,6, 10-15	
The supplementary search report has been based on the last set of claims valid and available at the start of the search.			
Place of search <b>MUNICH</b>		Date of completion of the search <b>22 November 2002</b>	Examiner <b>Trifilieff-Riolo, S</b>
<b>CATEGORY OF CITED DOCUMENTS</b> X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

2

EPO FORM 1503 03.02 (P04C04)

**ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.**

EP 00 94 6393

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on  
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

22-11-2002

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
DE 4142366	A	24-06-1993	DE	4123341 A1	21-01-1993
			DE	4142366 A1	24-06-1993
			CA	2073841 A1	16-01-1993
			EP	0529253 A1	03-03-1993
			JP	5247074 A	24-09-1993
			MX	9204094 A1	31-03-1994
			US	5519138 A	21-05-1996
EP 0556789	A	25-08-1993	DE	4204968 A1	26-08-1993
			DE	4219534 A1	16-12-1993
			CA	2089689 A1	20-08-1993
			EP	0556789 A2	25-08-1993
			JP	6001771 A	11-01-1994
WO 0016773	A	30-03-2000	FR	2783422 A1	24-03-2000
			AU	5522399 A	10-04-2000
			WO	0016773 A1	30-03-2000
WO 0002543	A	20-01-2000	AU	753486 B2	17-10-2002
			AU	5034999 A	01-02-2000
			BR	9912021 A	03-04-2001
			CA	2336822 A1	20-01-2000
			CN	1312715 T	12-09-2001
			WO	0002543 A2	20-01-2000
			EP	1096932 A2	09-05-2001
			HU	0102828 A2	29-04-2002
			JP	2002520274 T	09-07-2002
			NO	20010113 A	09-03-2001
			PL	345897 A1	14-01-2002
			SK	312001 A3	11-06-2001
			TR	200100062 T2	21-06-2001
			ZA	200100232 A	09-04-2002

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

9T  
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10/03/398  
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APR 29 2002  
TECH CENTER 1600/2000

Applicant's or agent's file reference 2624WO0P	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/JP00/04830	International filing date (day/month/year) 19 July 2000 (19.07.00)	Priority date (day/month/year) 21 July 1999 (21.07.99)
International Patent Classification (IPC) or national classification and IPC A61K 45/00, 31/4188, 31/4245, A61P 25/28, 9/10		
Applicant TAKEDA CHEMICAL INDUSTRIES, LTD.		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>5</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of _____ sheets.</p>
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>

Date of submission of the demand 23 August 2000 (23.08.00)	Date of completion of this report 11 June 2001 (11.06.2001)
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.



# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/JP00/04830

## I. Basis of the report

### 1. With regard to the **elements** of the international application:\*

- ☒ the international application as originally filed
- ☐ the description:  
 pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the claims:  
 pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, as amended (together with any statement under Article 19  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the drawings:  
 pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the sequence listing part of the description:  
 pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

### 2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

### 3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

### 4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/fig \_\_\_\_\_

### 5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/JP00/04830

## III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 14-15

because:

- ☒ the said international application, or the said claims Nos. 14-15  
relate to the following subject matter which does not require an international preliminary examination (*specify*):

The subject matters of claims 14 and 15 "relate to a method for treatment of the human body by therapy," which does not require an international preliminary examination by the International Preliminary Examining Authority in accordance with PCT Article 34(4)(a)(i) and Rule 67.1(iv).

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_  
are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported  
by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for said claims Nos. 14-15

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/JP00/04830

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)	Claims	1-13,16-17	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-13,16-17	NO
Industrial applicability (IA)	Claims	1-13,16-17	YES
	Claims		NO

**2. Citations and explanations**

Document 1: EP, 425921, A1 (Takeda Chemical Industries, Ltd.), 8 May, 1991 (08.05.91)

Document 2: EP, 459136, A1 (Takeda Chemical Industries, Ltd.), 4 December, 1991 (04.12.91), & US, 5328919, A

Document 3: "Crisis and Recurrence of Cerebrovascular Diseases and Prevention Thereof (in Japanese)," (Masatoshi Fujishima), Igakuno Ayumi, Ishiyaku Shuppan K.K., 23 January, 1999 (23.01.99), Vol. 188, No. 4, pages 217-222

Document 4: "Therapeutic effects of imidapril on cerebral lesions observed by magnetic resonance imaging in malignant stroke-prone spontaneously hypertensive rats," (Masaya Takahashi et al.), Journal of Hypertension, 1994, Vol. 12, No. 7, pages 761-768

Document 5: "Rehabilitation of Cerebral Infarction Patients - Functional Evaluation and How to Promote Rehabilitation -," (Tsuneo Hasegawa), Science of Cerebral Hemorrhage in the CT and MRI Age - New Diagnostic and Therapeutic System - (in Japanese), K.K. Nihon Rinshosha, 1993, Vol. 1, pages 505-508

**Claims 1-13, 16 and 17**

Documents 1 and 2 respectively describe the compounds having angiotensin II antagonism described in claims 5-9 of the present application, and also describe that the compounds are used for therapy of cerebral hemorrhage.

Document 3 describes that the risk factors of cerebral hemorrhage recurrence are not basically different from the risk factors of crisis.

Document 4 describes that imidapril, an ACE inhibitor, has an effect of preventing the recurrence of cerebral hemorrhage.

Document 5 describes neuropathic symptoms, dyskinesia, pathergasia, daily life action disorders and the like as aftereffects of cerebrovascular diseases.

As described in document 3, it is considered that the risk factors of cerebral hemorrhage recurrence are not basically different from the risk factors of crisis, and as described in document 4, it is considered that the ACE inhibitor as an antihypertensive agent capable of inhibiting the renin angiotensin series and inhibiting the action of angiotensin II like the compounds described in documents 1 and 2 are effective not only for therapy of cerebral hemorrhage but also for preventing recurrence of cerebral hemorrhage. So, it is considered to be obvious for a person skilled in the art to use the compounds used for therapy of cerebrovascular diseases also for not only therapy of cerebrovascular diseases but also for preventing recurrence of cerebrovascular diseases as described in documents 1 and 2.

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/JP00/04830

## Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V (Citations and explanations):

Furthermore, it is also considered to be obvious for a person skilled in the art to use them for the aftereffects as described in document 5.

The specification of the present application does not include the description for particularly supporting that the drugs described in claims 1-13, 16 and 17 are useful for preventing recurrence of cerebrovascular diseases or as agents for improving their aftereffects or inhibiting the evolution thereof.

So, the subject matters of claims 1-13, 16 and 17 do not appear to involve an inventive step.

9T  
Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 2624WO0P	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/JP00/04830	International filing date (day/month/year) 19 July 2000 (19.07.00)	Priority date (day/month/year) 21 July 1999 (21.07.99)
International Patent Classification (IPC) or national classification and IPC A61K 45/00, 31/4188, 31/4245, A61P 25/28, 9/10		
Applicant TAKEDA CHEMICAL INDUSTRIES, LTD.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of <u>5</u> sheets, including this cover sheet.  <input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).  These annexes consist of a total of _____ sheets.
3. This report contains indications relating to the following items:  I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application

Date of submission of the demand 23 August 2000 (23.08.00)	Date of completion of this report 11 June 2001 (11.06.2001)
Name and mailing address of the IPEA/JP  Facsimile No.	Authorized officer  Telephone No.

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/JP00/04830

## I. Basis of the report

### 1. With regard to the elements of the international application:\*

- ☒ the international application as originally filed
- ☐ the description:  
 pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the claims:  
 pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, as amended (together with any statement under Article 19  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the drawings:  
 pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the sequence listing part of the description:  
 pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

### 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

### 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

### 4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/fig \_\_\_\_\_

### 5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

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## III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 14-15

because:

☒ the said international application, or the said claims Nos. 14-15 relate to the following subject matter which does not require an international preliminary examination (*specify*):

The subject matters of claims 14 and 15 "relate to a method for treatment of the human body by therapy," which does not require an international preliminary examination by the International Preliminary Examining Authority in accordance with PCT Article 34(4)(a)(i) and Rule 67.1(iv).

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 14-15

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)	Claims	1-13,16-17	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-13,16-17	NO
Industrial applicability (IA)	Claims	1-13,16-17	YES
	Claims		NO

**2. Citations and explanations**

Document 1: EP, 425921, A1 (Takeda Chemical Industries, Ltd.), 8 May, 1991 (08.05.91)  
Document 2: EP, 459136, A1 (Takeda Chemical Industries, Ltd.), 4 December, 1991 (04.12.91), & US, 5328919, A

Document 3: "Crisis and Recurrence of Cerebrovascular Diseases and Prevention Thereof (in Japanese)," (Masatoshi Fujishima), Igakuno Ayumi, Ishiyaku Shuppan K.K., 23 January, 1999 (23.01.99), Vol. 188, No. 4, pages 217-222

Document 4: "Therapeutic effects of imidapril on cerebral lesions observed by magnetic resonance imaging in malignant stroke-prone spontaneously hypertensive rats," (Masaya Takahashi et al.), Journal of Hypertension, 1994, Vol. 12, No. 7, pages 761-768

Document 5: "Rehabilitation of Cerebral Infarction. Patients - Functional Evaluation and How to Promote Rehabilitation -," (Tsuneo Hasegawa), Science of Cerebral Hemorrhage in the CT and MRI Age - New Diagnostic and Therapeutic System - (in Japanese), K.K. Nihon Rinshosha, 1993, Vol. 1, pages 505-508

**Claims 1-13, 16 and 17**

Documents 1 and 2 respectively describe the compounds having angiotensin II antagonism described in claims 5-9 of the present application, and also describe that the compounds are used for therapy of cerebral hemorrhage.

Document 3 describes that the risk factors of cerebral hemorrhage recurrence are not basically different from the risk factors of crisis.

Document 4 describes that imidapril, an ACE inhibitor, has an effect of preventing the recurrence of cerebral hemorrhage.

Document 5 describes neuropathic symptoms, dyskinesia, pathergasia, daily life action disorders and the like as aftereffects of cerebrovascular diseases.

As described in document 3, it is considered that the risk factors of cerebral hemorrhage recurrence are not basically different from the risk factors of crisis, and as described in document 4, it is considered that the ACE inhibitor as an antihypertensive agent capable of inhibiting the renin angiotensin series and inhibiting the action of angiotensin II like the compounds described in documents 1 and 2 are effective not only for therapy of cerebral hemorrhage but also for preventing recurrence of cerebral hemorrhage. So, it is considered to be obvious for a person skilled in the art to use the compounds used for therapy of cerebrovascular diseases also for not only therapy of cerebrovascular diseases but also for preventing recurrence of cerebrovascular diseases as described in documents 1 and 2.



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**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V (Citations and explanations):

Furthermore, it is also considered to be obvious for a person skilled in the art to use them for the aftereffects as described in document 5.

The specification of the present application does not include the description for particularly supporting that the drugs described in claims 1-13, 16 and 17 are useful for preventing recurrence of cerebrovascular diseases or as agents for improving their aftereffects or inhibiting the evolution thereof.

So, the subject matters of claims 1-13, 16 and 17 do not appear to involve an inventive step.